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Anticoagulation upon hospital discharge in 2013: a retrospective analysis

MASTERARBEIT

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Contents

1. Abstract

Introduction

Direct oral anticoagulants have become an attractive option for many patients requiring oral anticoagulation. For patients with non-valvular atrial fibrillation current guidelines propose their preferential use based on the results of large randomized trials. However, when applying those results to non-selected patients with multiple medical conditions in “real world” settings caution is prudent because the complication rate in these patients may be higher than in the study populations. The aims of this study were a) to assess the overall prevalence of anticoagulation in patients discharged in 2013 after being hospitalized for a variety of medical conditions and b) to analyse the selection of various oral anticoagulation regimens under “real world” conditions in the context of diverse comorbidities.

Methods

This study was designed as retrospective analysis of patients discharged from the medical inpatient service at the University Hospital of Zurich in 2013. Patients receiving anticoagulation therapy were identified by codes of the anatomical therapeutic chemical classification system of their discharge medications using a computerized search algorithm. Medications and patient characteristics were extracted from the electronic medical record.

Results

Between January 1 and December 31 1439 discharge reports were generated by the general internal medicine service, of which 304 (21.1%) were on patients receiving therapeutic anticoagulation. Out of these, 228 patients received oral anticoagulants: 204 (89.5%) vitamin K antagonists and 24 (10.5%) the direct oral anticoagulant rivaroxaban. Patients on rivaroxaban tended to have fewer diagnoses and discharge medications, better renal function and shorter hospital stays, but the differences to the patients on vitamin K antagonists were not statistically significant, possibly due to the relatively low number of patients receiving rivaroxaban.

Conclusions

In a “real world” setting 21.1% of general internal medicine patients were discharged on anticoagulation therapy after hospitalization for a variety of conditions. The preferential use of vitamin K antagonists in 89.5% of orally anticoagulated patients likely reflects a combination of physicians’ extensive experience and familiarity with vitamin K antagonists in addition to patient characteristics and clinical indications. The role of clinical patient characteristics on anticoagulant choice remains to be clarified.

2. Abbreviations

AF	Atrial Fibrillation
AHA/ACC/HRS	American College of Cardiology / American Heart Association / Heart Rhythm Society
ATC-code	Anatomical Therapeutic Chemical Classification System
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration Equation
DOACs	Direct Oral Anticoagulants
DVT	Deep Vein Thrombosis
eGFR	Estimated Glomerular Filtration Rate
EHRA	European Heart Rhythm Association
ESC	European Society of Cardiology
GFR	Glomerular Filtration Rate
ICU	Intensive Care Unit
INR	International Normalized Ratio
KISIM	Clinical Information System
MWU	Mann-Whitney-U
nvAF	Non-Valvular Atrial Fibrillation
OAK	Oral Anticoagulation
PE	Pulmonary Embolism
Swissmedic	Swiss Agency for Therapeutic Products
VKA	Vitamin K Antagonist
VTE	Venous Thromboembolism

3. Introduction

3.1. Background and Rationale

Thromboembolic events due to atrial fibrillation (AF) and venous thromboembolism (VTE) are common and major contributors to morbidity and mortality worldwide. Currently, AF is estimated to affect 1.5-2% of the general population in the developed world (1). VTE, which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most frequent cardiovascular disease with an annual incidence of 100-200/100'000 people (2). Death or chronic disability due to thromboembolic events can be reduced by anticoagulation therapy (1, 3).

For many decades, vitamin K antagonists (VKAs) were the only oral anticoagulants (OAKs). VKA, as for example warfarin or phenprocoumon, are well-studied and have proven efficacy. VKA are appreciated because of the extensive experience gained over the last 50 years. Nonetheless, there are several disadvantages, like the narrow therapeutic window, drug-drug or drug-food interactions, the wide range of individual dosing requirements and the necessity of monitoring the international normalized ratio (INR) (4).

More recently, direct oral anticoagulants (DOACs) have become an attractive therapeutic option to treat and reduce the risk of thromboembolic events. In Switzerland, rivaroxaban was the first DOAC indicated for stroke and thromboembolism prevention licensed by the Swiss Agency for Therapeutic Products (Swissmedic) (5). Rivaroxaban was approved in 2008, followed by apixaban in 2011, dabigatran in 2012 and most recently edoxaban in 2015.

The indications for rivaroxaban (Xarelto®) (6), apixaban (Eliquis®) (7), dabigatran (Pradaxa®) (8) and edoxaban (Lixiana®) (9) are the reduction of the risk for stroke and thromboembolism in patients with non-valvular atrial fibrillation (nvAF) and the treatment and the prevention of DVT und PE. DOACs are not indicated for patients with mechanical heart valves. Rivaroxaban and apixaban are further indicated for the prevention of thromboembolism after hip or knee surgery.

The effects of DOACs in patients with nvAF were investigated in several large-scale randomized phase III trials. The RE-LY study (10, 11) examined dabigatran, the ARISTOTLE study (12) apixaban and the ROCKET study (13) rivaroxaban. The efficacy of edoxaban was studied in the ENGAGE-AF study (14). In these studies, DOACs were compared with warfarin. The primary outcomes were stroke or systemic embolism. All of these four studies confirmed the non-inferiority of DOACs compared to VKAs in patients with nvAF.

DOAC treatment of patients with DVT was investigated in separate randomized trials. The direct thrombin inhibitor dabigatran was studied in the RE-COVER (15, 16) trial. The direct factor Xa inhibitors apixaban, rivaroxaban and edoxaban were studied separately in the AMPLIFY (apixaban) (17), in the EINSTEIN (rivaroxaban) (18, 19) and in the Hokusai-VTE (edoxaban) (20) tri-

als. These four studies were conducted in a non-inferiority design for DOACs versus warfarin. The efficacy outcome was recurrent VTE or fatal PE and the safety outcome was major bleeding. In summary, these studies showed the non-inferiority of DOACs compared with warfarin in terms of DVT treatment and indicated a lower risk of major bleeding (21).

The practical use of DOACs differs from VKAs in several aspects (22). In contrast to VKAs, DOACs are prescribed in a fixed dosing regimen without the need for therapeutic drug monitoring. An initial heparin bridging is not necessary because of the rapid onset of action within approximately three hours. There is also no heparin bridging needed before planned surgical intervention. However, a major problem is renal dysfunction. DOACs may accumulate in patients with low glomerular filtration rate (GFR). These patients have a higher risk of major bleeding, including haemorrhagic stroke as well as a higher risk of thromboembolic events (23, 24).

Comorbid conditions are more common with increasing age. Nevertheless, DOACs showed even in elderly adults equal or greater efficacy than conventional anticoagulation therapy (25). The CHA_2DS_2-VASc-score and the HAS-BLED scores are based on various clinical characteristics and comorbid conditions and can be helpful to identify patients who benefit from anticoagulation therapy. However, there is ongoing discussion about the limited experience with DOACs in patients with complex and multiple medical disorders who may not have been included in the clinical trials on which the scoring systems are based. The aim of the present work was to analyse the anticoagulation regimens under “real world” conditions with the following study questions:

1. How frequently were patients discharged from our internal medical service on (oral) anticoagulation?
2. Which anticoagulation drugs were used?
3. Is the choice of anticoagulant related to patient characteristics?

3.2. Pharmacology of anticoagulants

VKAs and DOACs impact on the coagulation cascade by different mechanisms of action (Figure 1). VKA are coumarin derivatives and inhibit the synthesis of the vitamin K dependent coagulation factors II (prothrombin), VII, IX and X in the liver. VKA displace vitamin K in specific enzyme systems and do not influence coagulation factors which have already been synthesized. Phenprocoumon is a commonly used VKA in Switzerland. It takes 2-3 days before the action can be appreciated in the blood and requires frequent monitoring of the INR which should be between 2 and 3 for most indications. The half-life of phenprocoumon is around 160 hours and the excretion is in 35% renal (26).

Rivaroxaban, apixaban, edoxaban and dabigatran bind reversibly to the catalytic pocket of free or clot-bound coagulation factors. Therefore, they have a shorter time to onset of action compared to VKAs. Rivaroxaban is a factor Xa inhibitor. The bioavailability varies between 66%

when taken without food and almost 100% when taken with food. The time to onset of action is between 2 -4 h. The half-life is estimated between 5 -9 h in young and 11 – 13 h in elderly people. A third of the drug is cleared renally (6).

Apixaban is also a factor Xa inhibitor. Its bioavailability is about 50%. The clearance is in 27% renal. Therefore, the dosing of apixaban depends on the kidney function as well as patients' age and weight. The time to onset of action varies between 3 - 4 h and the elimination half-life is about 12 h (7).

The recently introduced factor Xa inhibitor edoxaban has a bioavailability of 62%. The ratio of non-renal to renal clearance is 50:50 and the onset of action is within 1 - 2 h with an elimination half-life of 10 – 14 h (9).

In contrast to these factor Xa inhibiting DOACs, dabigatran is a prodrug that requires hepatic conversion to pharmacologically active acyl glucuronides which inhibit thrombin (coagulation factor IIa). Dabigatran's onset of action is between 0.5 – 2 h with a half-life between 12 – 14 h and a mostly renal clearance (8).

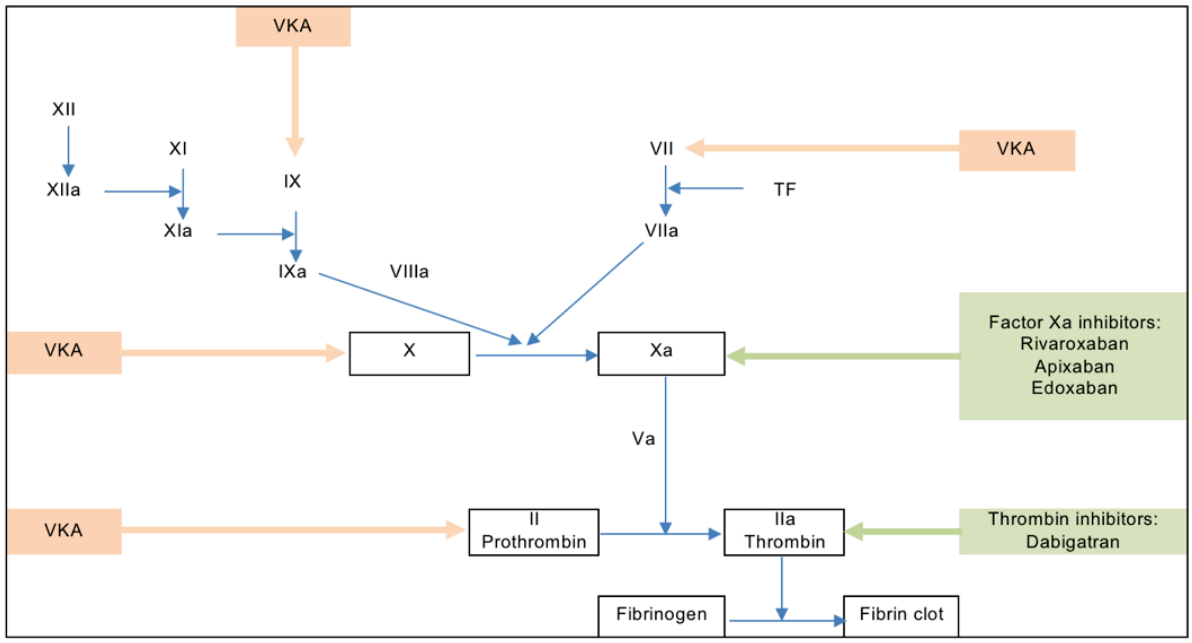

Figure 1: Points of action of oral anticoagulants in the coagulation cascade. (TF = tissue factor)

4. Methods

4.1. Setting

The University Hospital of Zurich is a Swiss teaching hospital providing highest level medical care in all specialties. Most of the patients admitted to the internal medicine service enter the hospital via the emergency unit with diverse medical conditions. Typically, many of these patients are elderly and/or suffer from several chronic conditions that require the coordinated care of various surgical and medical specialties.

4.2. Study design

This study was designed as a retrospective assessment of anticoagulant use in hospitalized patients of the internal medicine service at the University Hospital of Zurich. The study was based on a medical record review of the clinical information system (KISIM). The determinant of the study was defined as patients receiving anticoagulation therapy upon discharge between 01.01.2013 – 31.12.2013.

4.3. Sample

All patients discharged on anticoagulation therapy from the internal medicine service of the University Hospital Zurich between 01.01.2013 – 31.12.2013 were identified per documentation of the anticoagulation drug in the discharge report. This information was collected using a computerized search algorithm of the electronic medical records (KISIM, www.cistec.com) which categorized the anticoagulation according to the codes of the Anatomical Therapeutic Chemical Classification System (ATC-code). For better readability in the following text the word “discharge summary” is substituted by “patient”, although an exceptional patient may have been admitted to our hospital more than once in 2013. The following ATC-codes in the discharge medication defined the anticoagulation status:

B	blood and blood forming organs
B01	antithrombotic agents
B01AA	vitamin K antagonists
B01AB	heparin group
B01AE	direct thrombin inhibitors
B01AF	direct factor Xa inhibitors
B01AX	other antithrombotic agents

Patients with the explicit directive in the clinical information system that no clinical information may be used for research and patients under the age of 18 years were excluded.

4.4. Data collection

In collaboration with the information technology unit of the University Hospital Zurich a search algorithm was designed to identify valid and not restricted hospital discharge summaries with the defined ATC-codes. The following patient data were extracted from the clinical information system onto a Microsoft Excel (Microsoft Excel, Version 15.18. Redmond, Washington: Microsoft Corp.) spreadsheet: patient number, case number, age, sex, length of hospital stay, discharge drug list, type of anticoagulant therapy and total number of diagnosis items in the discharge summary. Further information on renal function and OAK therapy prior to admission was collected by reviewing the medical records and laboratory tests of each patient. For quantifying and comparing the renal function, the serum concentration of creatinine as well as the estimated glomerular filtration rate (eGFR), using the chronic kidney disease epidemiology collaboration equation (CKD-EPI) 2009, were analysed.

4.5. Statistical Analyses

Statistical analyses and data visualisations were done with SPSS (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). Descriptive statistics with confidence intervals were used for assessing the proportion of anticoagulated patients out of all patients discharged from the internal medicine service in 2013. Secondary analyses addressed the choice of various anticoagulation regimens and its potential correlation with patient characteristics. Therefore, patient characteristics such as age, gender, kidney function and the length of hospital stay were studied, as well as the total number of drugs, total number of diagnoses and OAK therapy on admission. The data were tested for normal distribution by graphic interpretation in combination with the Shapiro-Wilk test. Chi-square test was used to compare categorical data. To test whether there were significant differences between continuous data the Mann-Whitney-U (MWU) test was used. Significant differences were based on a p-value < 0.05.

4.6. Patient Privacy and Ethical Considerations

The Excel spreadsheet contained exclusively anonymous patient information and the reported results preclude the identification of individual patients. According to requirements, the study was approved by the ethics committee Zurich (“Kantonale Ethikkommission Zürich”; www.kek.zh.ch, reference number KEK-ZH-Nr. 2014-0435).

5. Results

5.1. Patient identification

From January 01, 2013 through December 31, 2013 1439 discharge reports from the internal medicine service were identified, 305 of which contained anticoagulant medication(s). One patient aged under 18 years was excluded. 76 patients received parenteral anticoagulant drugs like heparin, dalteparin, enoxaparin, nadroparin or fondaparinux and were therefore not analysed as our study focused exclusively on OAK regimens. In total, 228 patients on OAK were included for further analysis (Figure 2).

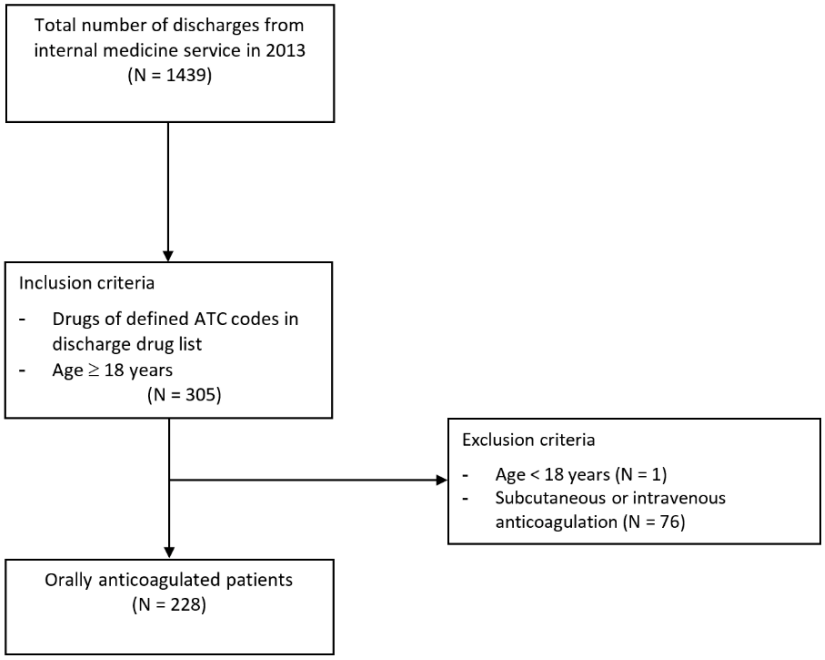

Figure 2: Study cohort.

5.2. Primary outcome

The main finding of this study is that out of 1439 discharge records in the year 2013, a total of 304 (21.1%) documented either oral or parenteral anticoagulation therapy. Since the great majority of patients only had one hospitalisation during 2013, this result indicates that approximately 1/5 of patients discharged from our general internal medicine service received anticoagulation therapy: 75% of these (n=228, i.e. 15.8% of the total number of records) were discharged on OAK therapy with VKA or DOACs, whereas 25% (n=76, i.e. 5.3% of the total number of records) were discharged on various parenteral anticoagulation regimens. In 2013 204 (89.5%) of 228 discharge records) documented VKA, almost exclusively phenprocoumon; one single patient was treated with acenocoumarol. Rivaroxaban was the only DOAC prescribed in 24 discharge reports, accounting for 10.5% of all orally anticoagulated patients and 1.7% of all discharged patients during 2013.

5.3. Gender

Among the 204 patients with VKA in the discharge drug list, 114 (55.9%) were men. Out of the 24 patients on rivaroxaban, 11 (45.8%) were men. The difference between men and women is not statistically significant (chi square test, P=0.39).

5.4. Age

In the rivaroxaban group the age ranged from 51 to 91 years. 2 (8.3%) patients were younger than 65 years, 6 (25.0%) between 65-75 years, 11 (45.8%) between 75-85 years and 5 (20.8%) were aged over 85 years. In the VKA group, the age distribution ranged from 25 years to 99 years. The age group ≤65 years included 45 (22.0%) patients and the age group 65-75 years included 46 (22.5%) patients. In the next higher age group 75-85 years were 75 (36.8%) patients and 38 (18.6%) patients were aged ≥ 85 years. Regarding the mean of the rivaroxaban and the VKA group, there was no significant difference (MWU-test, P=0.33). The mean age in the rivaroxaban group was 76.1±10.6 years (median 79; interquartile range 76.0 - 84.0). The mean age of the VKA group was 73.2±13.9 years (median 76; interquartile range 65.25 - 82.0).

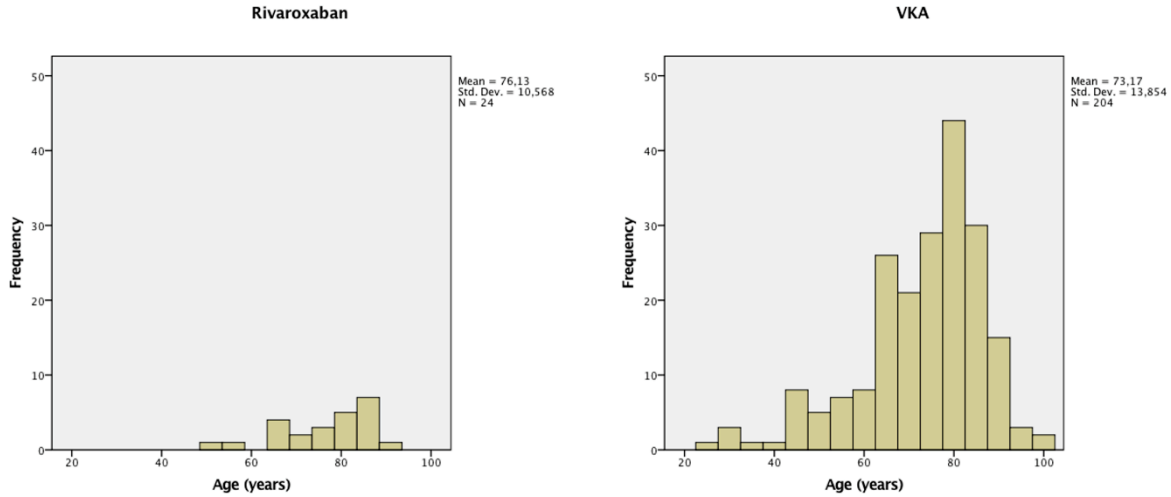

Figure 3: Frequency distribution of anticoagulation according to age and treatment group.

5.5. Total number of drugs

Patients on rivaroxaban therapy had a total of 8.9±4.3 drugs (median 7; interquartile range 6.0 - 12.5) in their discharge report, patients on VKA therapy 10.3±4.7 different drugs (median 10; interquartile range 7.0 - 13.0) respectively. The total number of drugs did not significantly correlate with DOAC or VKA therapy (MWU-test, P=0.18).

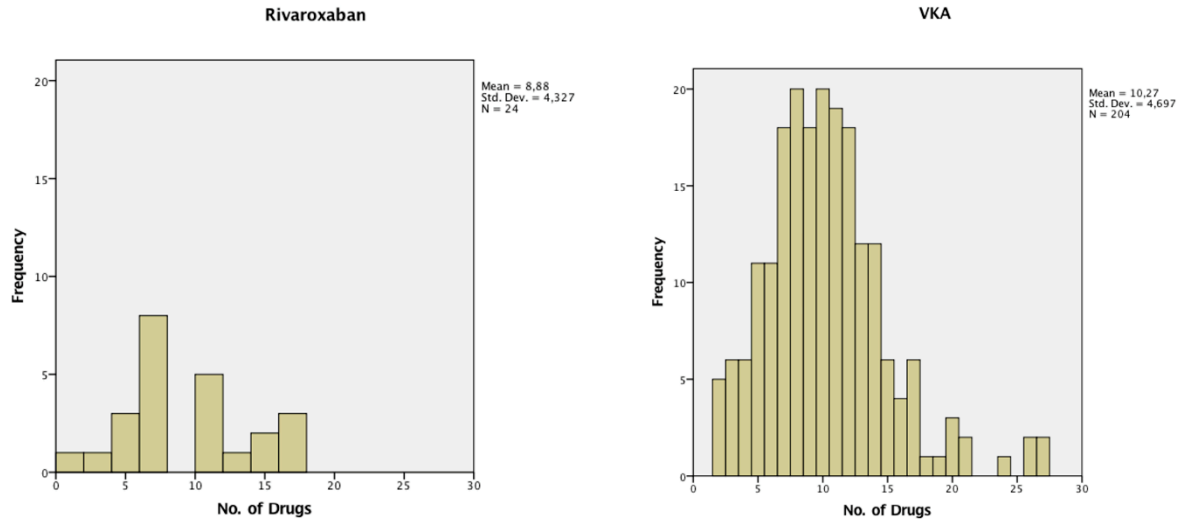

Figure 4: Frequency distribution of anticoagulation according to total number of drugs and treatment group.

5.6. Total number of diagnoses

Patients anticoagulated with rivaroxaban had a mean number of 8.1±2.7 diagnoses (median 8.5; interquartile range 6.0-10.0). The number of diagnoses in the group of patients with VKA averages 8.3±3.1 (median 8, interquartile range 6.0-10.75) indicating that there is no significant difference (MWU-test, P=0.90).

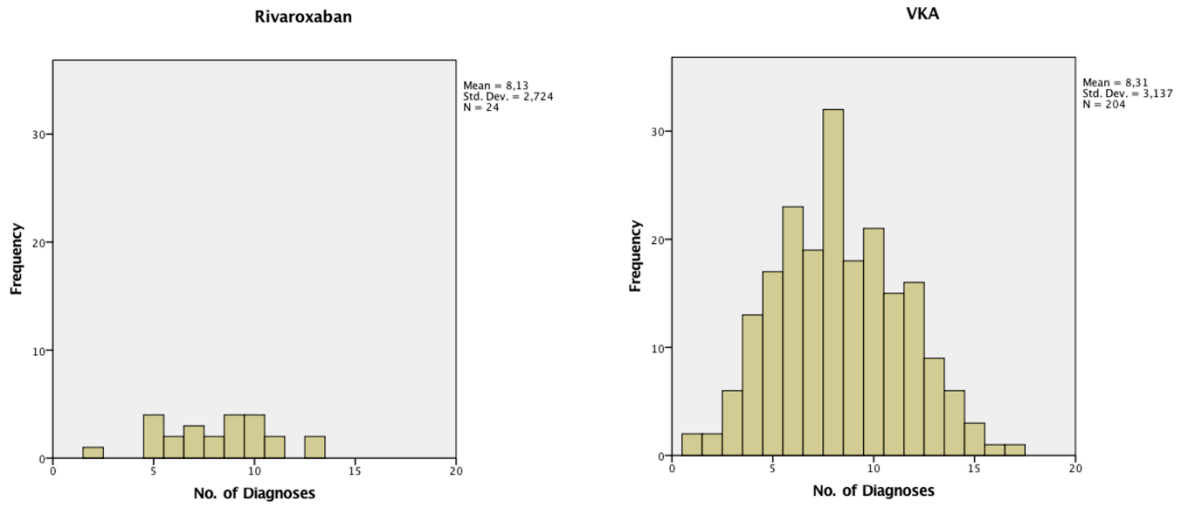

Figure 5: Frequency distribution of anticoagulation according to total number of diagnoses and treatment group.

5.7. Length of hospital stay

On average, patients on rivaroxaban stayed 10.0±9.4 days (median 8.0; interquartile range 4.0–13.0) in the hospital, whereas patients on VKA stayed 12.7±12.8 days (median 8.0; interquartile range 4.25–17.0), difference not significant (MWU-test, P=0.27). The histogram of the length of stay is considerably skewed contradicting a normal distribution. In both the rivaroxaban and the VKA group, there is a peak around 8 days and with a subsequent sharp decline.

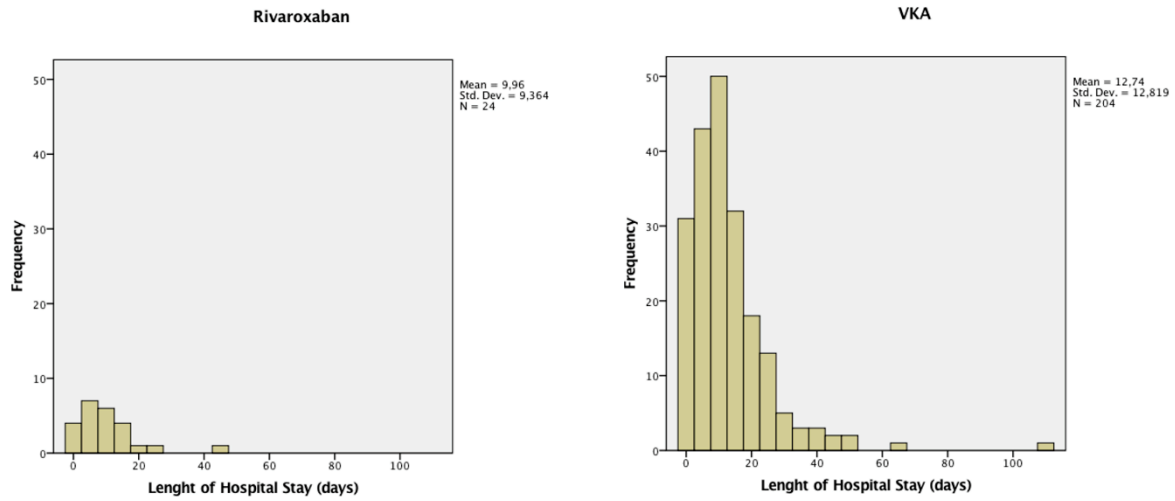

Figure 6: Frequency distribution of anticoagulation according to length of hospital stay and treatment group.

5.8. Renal function

Patients receiving rivaroxaban at discharge (n=24 laboratory tests) had a mean eGFR of 60.7±5.0 ml/min/1.73m^2 (median 59; interquartile range 40.25-73.0) and a mean serum creatinine concentration of 103.0±9.6 µmol/l (median 86.5; interquartile range 68.5-125.75). In the VKA group the mean eGFR (n=192 laboratory tests) was 51.8±1.8 ml/min/1.73m^2 (median 49.5; interquartile range 32.0-68.75) and the mean creatinine level (n=198 laboratory tests) was 131.5±5.1 µmol/l (median 110; interquartile range 80.0 – 155.25). Patients discharged on VKA did not have a significantly lower renal function as judged by lower eGFR values (MWU-test, P=0.09) as well as no higher serum creatinine concentration (MWU-test, P=0.33).

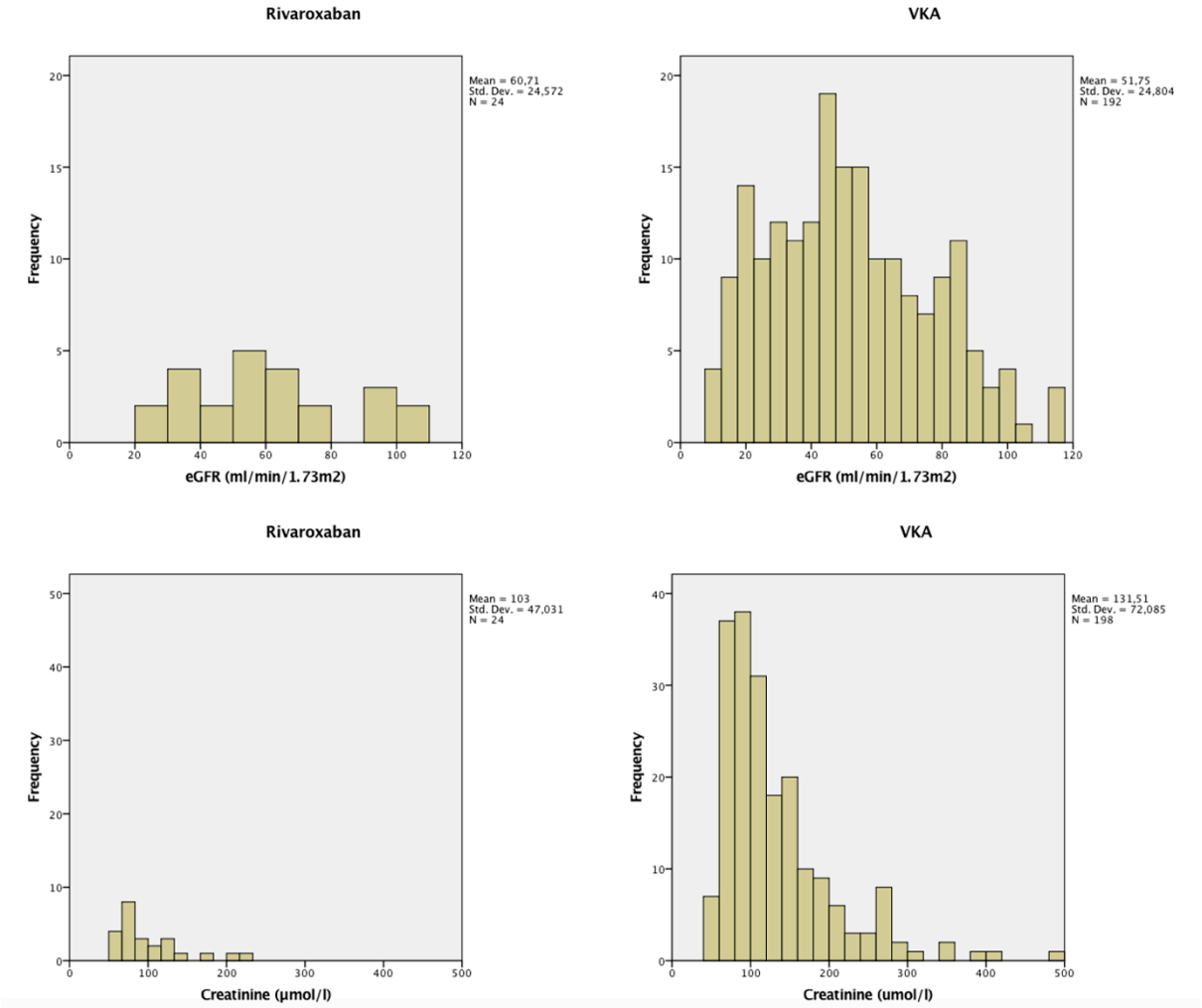

Figure 7: eGFR and creatinine levels according to treatment group.

Table 1: Characteristics of orally anticoagulated patients according to treatment group. (SD = standard deviation)

	Rivaroxaban	VKA	P-value
No. of patients	24	204	
Sex			P=0.39
Male	11	114	
Female	13	90	
Age (years)			
Mean±SD	76.1±10.6	73.2±13.9	P=0.33
Median	79	76	
Interquartile range	76.0-84.0	65.25 – 82.0	
< 65 yr (%)	2 (8.3)	45 (22.0)	
65 - < 75 yr (%)	6 (25.0)	46 (22.5)	
75 - < 85 yr (%)	11 (45.8)	75 (36.8)	
≥ 85 yr (%)	5 (20.8)	38 (18.6)	
Total no. of drugs			
Mean±SD	8.9±4.3	10.3±4.7	P=0.18
Median	7	10	
Interquartile range	6.0–12.5	7.0–13.0	
Total no. of diagnoses			
Mean±SD	8.1±2.7	8.3±3.1	P=0.90
Median	8.5	8	
Interquartile range	6-10	6–10.75	
Length of hospital stay (days)			
Mean±SD	10.0±9.4	12.7±12.8	P=0.27
Median	8	10	
Interquartile range	4.0–13.0	4.25–17.0	
eGFR (ml/min/1.73m^2)			
Mean±SD	60.7±5.0	51.8±1.8	P=0.09
Median	59	49.5	
Interquartile range	40.25-73.0	32.0-68.75	
Creatinine (µmol/l)			
Mean±SD	103.0±9.6	131.5±5.1	P=0.33
Median	86.5	110	
Interquartile range	68.5-125.75	80.0-155.25	

6. Discussion

6.1. Oral anticoagulation at hospital discharge in 2013

In this retrospective study the frequency and choice of anticoagulants was analysed in patients discharged from an in-patient general medicine service after treatment of a variety of medical conditions, including, but not limited to thromboembolic complications and atrial fibrillation. In 2013 89.5% of orally anticoagulated patients were discharged on a traditional VKA regimen and 10.5% were discharged on rivaroxaban which at the time was the only DOAC on the hospital formulary. The use of OAK is influenced by changes of guidelines and recommendations for anticoagulation therapy. In 2011 DOACs were included in the update of the guidelines on the management of patients with AF of the American College of Cardiology / American Heart Association / Heart Rhythm Society (AHA/ACC/HRS) (27) without specific recommendations for the choice of anticoagulant. One year later, the ESC guideline for the management of AF stated, that DOACs “should be considered instead of adjusted-dose VKA for most patients with AF” (1). In April 2013 the EHRA published a practical guide on the use of new OAK in patients with nvAF (4). With increasing experience in the practical use of DOACs the AHA/ACC/HRS published updated practice guidelines for the management of patients with nvAF in 2014 that recommended DOACs for patients unable to maintain a therapeutic INR on warfarin (28). The 2015 guidelines of the ESC recommend for the first time the preferential use of DOACs instead of VKA for stroke prevention in patients with nvAF based on the reduced bleeding risk compared to warfarin in large randomized clinical trials (29).

However, caution is needed when transferring results of the randomized trials into real world setting: clinical trial results are derived from defined study populations that may not be identical to unselected patients in general clinical practise. This is especially true when these drugs are used in elderly patients with multiple diagnoses and often borderline renal function. Furthermore, the large-scaled studies compared DOACs with warfarin, which is world-wide the most prescribed VKA (30). In Europe phenprocoumon and acenocoumarol are more commonly used which act in the same way as warfarin but with different pharmacokinetics.

6.2. Comparison of the present results with the literature

The prescription patterns of OAK have previously been studied on a large scale. Lauffenburger et. al. (31) and Desai et. al. (32) studied patients with nvAF initiating anticoagulation therapy, Lauffenburger et. al. between October 2010 and December 2012 and Desai et. al. between 2010 and 2013. The results of Lauffenburger et. al. showed that out of 70498 patients initiating anticoagulation 30% got dabigatran and 8% rivaroxaban. Apixaban, FDA approved since December 2012, was not included in the study. The preferential use of dabigatran compared to rivaroxaban reflects the impact of the RELY-study which documented the efficacy and safety of

dabigatran. The study of Lauffenburger et. al. is consistent with our results that VKA is for many physicians still the drug of choice, as 62% of patients received warfarin. Desai et al. showed similar results. They reported that out of 45472 patients initiating an anticoagulation therapy 57.7% received warfarin, 32.8% dabigatran, 9.3% rivaroxaban and 0.1% apixaban.

Barnes et. al. (33) analysed the oral anticoagulation use in ambulatory visits for AF and venous thromboembolism in the United States. Out of around 2.5 million treatment visits in 2013, warfarin was used in 75%, in 25% DOACs. Rivaroxaban was the most commonly prescribed DOAC with a rate of 57%, followed by dabigatran with 35% and apixaban with 7.5%. The higher proportion of patients treated with DOACs compared to our results is most likely explained by the ambulatory setting of the study in contrast to our inpatient setting. Nevertheless, their results are in line with our findings that even in this study on non-hospitalized patients VKA were by far the most commonly prescribed OAK.

6.3. Determinants of oral anticoagulant selection

Before starting chronic oral anticoagulation therapy physicians have to evaluate three different possibilities: first, starting a therapy with VKA, second, starting with a DOAC and third, deciding against an OAK therapy due to contraindications and/or individual assessment of risk versus benefit. The choice between VKA and DOACs is likely to depend on patient factors like age, medications, co-morbid conditions, renal function and perceived bleeding risk. Therefore, we performed a pilot analysis of potentially relevant clinical features of patients on rivaroxaban versus phenprocoumon even though the small size of the rivaroxaban group is a limiting factor. Our data do not reveal significant differences between these two groups. However, patients receiving rivaroxaban tended to have less morbidity than patients on VKA: the number of diagnoses and medications tended to be lower, the renal function tended to be better and the duration of hospitalization tended to be shorter. Taken together these results suggest that rivaroxaban may have been prescribed in less severely ill patients. This hypothesis is consistent with the results of Desai et. al. (32) and Lauffenburger et. al. (31) despite the fact that they included only patients with nvAF and not with other clinical conditions like DVT and LE as in the present work. Desai et. al. showed that DOAC use was significantly associated with female sex, fewer concomitant medications and shorter hospital stays. Furthermore, patients with AF on anticoagulation with DOACs tended to be younger and healthier. Lauffenburger et. al. found that patients with greater bleeding and ischemic stroke risk were more likely to be treated with warfarin, possibly because INR monitoring is felt to improve patient adherence.

6.4. Renal failure and the use of DOACs

Since all DOACs are contraindicated in patients with renal failure, we tested the hypothesis that the selection of OAK was correlated with renal function. Rivaroxaban is contraindicated when the GFR is less than 15 ml/min (6). In our patients discharged on VKA the eGFR was between 10 and 117 ml/min/1.73m^2. Over 50% of them had an eGFR above 50 ml/min/1.73m^2 so that DOACs could have been used at normal dosage. The present work failed to demonstrate statistically significant differences of renal function between the patient groups. Nevertheless, the patients treated with rivaroxaban tended to have a better renal function suggesting that this important clinical characteristic may have an influence on anticoagulant choice (see above).

6.5. Limitations

The present retrospective analysis has several limitations. Patient selection was based on anticoagulation treatment at discharge and not on the indications of anticoagulation therapy. Hence, we did not exclude patients with valvular AF, mechanical heart valves, DVT or LE. Moreover, the number of patients without anticoagulation despite an indication is not known. Patients of the intensive care units (ICU) were only included if they had been transferred to the regular medical service prior to discharge. Due to the computerized search algorithm any patients transferred directly from the ICUs to outside institutions or patients dying in the intensive care units were not identified.

6.6. Future studies

It takes time until the results of the large scale clinical trials on defined populations are transferred into real world clinical practice. During the observation period of this study the restrictive use of these new drugs in elderly patients with multiple diagnoses seemed prudent. However, with increasing familiarity of physicians DOACs are likely to overtake VKA as the anticoagulants of choice for the most common indications non-valvular atrial fibrillation and venous thromboembolism, but VKA can be expected to retain an important role for individual patients with selected indications.

6.7. Conclusions

Our results show that 304 (21.1%) of 1439 of patients discharged in 2013 from our general medical service after hospitalization for a variety of conditions received anticoagulation. The only DOAC prescribed upon discharge was rivaroxaban in 10.5% of orally anticoagulated patients. Patients discharged on rivaroxaban were not statistically different from patients on VKA despite a trend suggesting a higher morbidity of patients on VKA. This hypothesis could be tested in future studies. Our main result, i.e. that in 2013 21.1% of general medicine patients were discharged from hospital on anticoagulation is consistent with current guidelines. The preferential use of VKA in 89.5% of orally anticoagulated patients likely reflects a combination of patient characteristics and clinical indications because in contrast to VKA DOACs are not approved for all indications. However, physician behaviour also needs to be taken into account as physicians are cautious when it comes to changing prescribing patterns. Therefore, observational studies in real world settings are an important adjunct to randomized clinical trials for the implementation of evidence-based guidelines into clinical practice.

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9. Statement

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Ich erkläre ausdrücklich, dass es sich bei der von mir im Rahmen des Studiengangs

Master of Medicine der Medizinischen Fakultät der Universität Zürich

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